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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,956	11/30/2001	Zairen Sun	9U 301 R1	2406

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ORIGENE TECHNOLOGIES, INCORPORATED
6 TAFT COURT
SUITE 100
ROCKVILLE, MD 20850

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	6

DATE MAILED: 10/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/996,956	Sun et al
Examiner	**Art Unit**
Ungar	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 1, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3, 5-13, 15-18, and 21-23* is/are pending in the application.

4a) Of the above, claim(s) *5-13, 15-17, and 21-23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3 and 18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Election filed July 1, 2003 (Paper No. 4) in response to the Office Action of April 9, 2003 (Paper No. 3) is acknowledged and has been entered. Claims 1-3, 5-13, 15-18, 21-23 are pending in the application and Claims 5-13, 15-17, 21-23 and all limitations in claim 18 draw to SEQ ID NO:3 have been withdrawn from further consideration by the examiner under 37 CAR 1.142(b) as being drawn to non-elected inventions. It is noted that due to the amendment of claim 3, claim 3 has been rejoined with Group 1. Claims 1, 2, 3, 18 are currently under prosecution.

2. The response (Paper No. 4) to the restriction requirement of April 9, 2003 has been received. Applicant has elected Group I, claims 1, 2, 18 for examination with traverse. The traversal is on the ground(s) that all of the groups involve related subject matter and are drawn to human prostate genes so that it would not be an undue burden on the examiner to carry out a search. The argument has been considered but has not been found persuasive because the literature search involved with the search of each sequence is extensive. It is an undue burden on the office to search more than one sequence because of the huge number of sequences now found in the sequence databases that must be searched and different searches and issues are involved in the examination of each group. Applicant further argues that the restriction between Group 1 and Group 2 is improper because SEQ ID NOS 1 and 3 are related sequences in that they arise from the same gene and are apparently either allelic or splice variants, one from the other. The argument has been considered but has not been found persuasive because the sequences are of different length and comprise different nucleic acid residues which must be separately searched and for

the reasons set forth above, this is an undue burden on the office. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

3. The specification on page 1 should be amended to reflect the status of the parent application.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

5. Claims 1, 2, 3 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The disclosed utilities for PR33a, SEQ ID NO:1 include the encoding of polypeptides and its application to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine. The specification teaches that the polynucleotide is differentially expressed in prostate cancer and is therefore useful in a variety of ways, including as a molecular marker, as a drug target and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determination, predisposition to diseases and conditions, especially relating to prostate cancer. (It is noted that there is no teaching of what SEQ ID NO:1 is compared to in order to determine differential expression. For example, it is

compared to normal prostate tissue, is it compared to expression in other tissues? Further there is no teaching of how the polynucleotide is differentially expressed, it is unknown whether, for example, it is overexpressed, underexpressed or expressed in a different compartment or is expressed in a mutated form, is it expressed in variable amounts in prostate cancer and more consistent amounts in normal prostate tissue, if in variable amounts, how variable are the amounts compared to expected normal variability, in other words is the variability significant?) In particular, identification of specific genes expressed in pathways physiologically relevant to prostate cancer permits the definition of functional and disease pathways, the delineation of targets in these pathways which are useful in diagnostic, therapeutic and clinical applications (p. 1. Lines 16-29). SEQ ID NO:1 is selectively expressed in prostate. The polynucleotide is useful as a prostate marker and probe because its occurrence in a sample indicates the presence of prostate cells and thus the polynucleotide has significant applications in diagnosis, therapy and related areas (p. 4, lines 10-18). In particular, detection and staging of prostate disease can be accomplished using polynucleotide probes (SEQ ID NO:1). Probes can be used *in vitro* on biopsies tissue as markers to identify and characterize premalignant tissues and cells, neoplasia, adenocarcinoma as well as in blood or other bodily fluids. Further, probes can be used for *in vivo* imaging according to conventional methodologies. Together with other known tests, differential diagnosis can be enhanced when Gleason grade and TNM are used in conjunction with methods of detection described herein. Together these methods provide more accurate disease diagnosis, disease progression and other information useful for determining therapy

and prognosis of cancer. Further, a number of genes and gene products have been associated with prostate cancer and metastasis and/or progression and such markers can be used in combination with the methods of the present invention to facilitate identifying, grading, staging, prognostication of conditions and diseases of the prostate (p. 27, lines 3-27). In addition to their use as tissue-selective markers and probes, the noncoding RNAs of the present invention can have one or more functions associated with known noncoding RNAs, including the functions displayed by the laundry list of molecules disclosed on pages 27-28. (It is noted that no particular function has been identified for noncoding RNA of SEQ ID NO:1.) Further PR33a contains Alu-type sequences in anti-sense orientation, making them useful as probes to detect and quantitate Alu sequences and as modulators of expressed Alu sequences (p. 28, lines 1-24). The polynucleotides of the invention can be utilized in therapeutic applications to treat diseases and conditions of the prostate. In particular, the polynucleotide can be used as naked DNA for vaccination or gene therapy (p. 28, lines 26-28) and delivery of the therapeutic agent can be achieved according to any effective method (p. 29, lines 8-10). Further, the specification teaches the sequence of SEQ ID NO:1 and discloses two Alu-type sequences in a reverse antisense orientation. On Northern blot the transcript is detected at about 5KD and expression of SEQ ID NO:1 is found in prostate but is absent or at very low levels, in brain, heart, kidney, spleen, liver, colon, lung, small intestine, muscle, stomach, testis, placenta, salivary gland, thyroid, adrenal gland, pancreas, ovary, uterus, skin, peripheral blood leucocytes, bone marrow, fetal brain and fetal liver. The polynucleotide is present in prostate cancer but in variable

amounts (para bridging pages 3-4). Given this statement, since it would be expected that SEQ ID NO:1 would be variably expressed in normal tissue as well, it is not possible to infer any nexus between the expression of SEQ ID NO:1 in normal prostate and prostate cancer tissue, especially since there is no teaching in the specification that expression of SEQ ID NO:1 was compared between normal prostate tissue and prostate cancer tissue. Further, the previous statement that SEQ ID NO:1 is differentially expressed in prostate cancer cells cannot be evaluated because there is no information as to what is meant by "differentially expressed" and there is no information that the differential expression is seen in prostate cancer tissue when compared with normal prostate tissue. Thus, the suggested "utility" drawn to "differential expression"is not an asserted utility since it cannot be used. Thus, neither the specification nor any art of record teaches what PR33a is, what it does do, they do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases. The asserted utilities for PR33a, such as it ability to encode a polypeptide apply to many unrelated polypeptide structures sequences. Further, its selective expression in prostate as compared with the low levels of mRNA expression in other tissues also applies to many unrelated polynucleotides such as PSA, PSMA, Prostate Cancer Marker 1 (see US 20020042062) and PAP. In addition, its use as a probe or modulator of Alu sequences also applies to all other sequences with Alu-type sequences in anti-sense orientation. Therefore these asserted utilities are not considered "specific" utilities, i.e. they are not specific to PR33a. Additional disclosed utilities are drawn to the noncoding RNAs which can have one or more functions associated with the laundry

list of known noncoding RNAs recited on pages 27-28. However, the specification does not disclose which particular function of the listed molecules can be attributed to SEQ ID NO:1. Thus, additional experimentation must be performed in order to determine what the particular functions of SEQ ID NO:1 are. Further, as drawn to the use of SEQ ID NO:1 include its use as a drug target and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determination of predisposition to diseases and conditions, its use for vaccination or gene therapy, especially relating to prostate cancer. These asserted utilities of PR33a are based on the assertion that PR33a (SEQ ID NO:1) is selectively expressed in prostate and the suggestion that SEQ ID NO:1 is differentially expressed/variably expressed in prostate cancer. Given the information in the specification, for the reasons set forth above, it is not possible to evaluate whether or not SEQ ID NO:1 is differentially expressed in primary prostate cancer cells as compared with normal prostate cells or whether the claimed polynucleotide could be used in any of the suggested methods. Further work must be done in order to establish a nexus between expression of SEQ ID NO:1 and prostate cancer, thus the invention does not have substantial utility. Further, the specification gives no information as to the source of the claimed SEQ ID NO:1. That is, it is not possible to determine from the information in the specification whether the sequence was isolated from primary prostate cells or whether it was isolated from a prostate cell line. Further, it is not possible to determine whether the "differential expression" referred to on page 1 or the "variable expression" referred to on page 4 were assayed in cell lines or primary tumor tissue. Without access to this information it is

not possible to evaluate the information in the specification or to determine a nexus between prostate cancer and the expression of SEQ ID NO:1. Since further work must be done in order to establish a nexus between expression of SEQ ID NO:1 and prostate cancer, the invention does not have substantial utility. Further, even if it were to be demonstrated that SEQ ID NO:1 is differentially expressed in primary prostate tumor compared to normal control, there is no teaching in the specification whether the differential expression is an up regulation or a down regulation or any of the other types of differential expression referred to above or even other types differential expression not referred to above. Thus, additional work must be done in order to determine what the differential expression might be and the claimed invention does not have substantial utility. The specification clearly states that SEQ ID NO:1 is a novel polynucleotide. Therefore, it is clear that SEQ ID NO:1 does not have a well established utility. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids. Because the claimed invention is not supported by a specific asserted utility, a substantial utility, a well established utility for the reasons set forth, credibility of any utility cannot be assessed.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall

set forth the best mode contemplated by the inventor of carrying out his invention."

7. Claims 1, 2, 3 and 18 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by a specific utility, a well established utility, a substantial utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 1, 2, 3 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The claims are drawn to SEQ ID NO:1, complements thereof and arrays comprising SEQ ID NO:1 or fragment probes thereof or complements thereof.

The specification teaches that as set forth above, that is, PR33a, SEQ ID NO:1 can be used for research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine. The polynucleotide is differentially expressed in prostate cancer and is therefore useful in a variety of ways, including as a molecular marker, as a drug target and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determination, predisposition to diseases and conditions, especially relating to prostate cancer (p. 1 lines 16-29). SEQ ID NO:1 is selectively expressed in prostate. The polynucleotide is useful as a prostate marker and probe because its occurrence in a sample indicates the presence

of prostate cells and thus the polynucleotide has significant applications in diagnosis, therapy and related areas (p. 4, lines 10-18). In addition to their use as tissue-selective markers and probes, the noncoding RNAs of the present invention can have one or more functions associated with known noncoding RNAs including the functions displayed by the laundry list of molecules disclosed on pages 27-28. Further PR33a contains Alu-type sequences in anti-sense orientation, making them useful as probes to detect and quantitate Alu sequences and as modulators of expressed Alu sequences (p. 28, lines 1-24).

In particular the specification teaches the sequence of SEQ ID NO:1 and discloses two Alu-type sequences in a reverse antisense orientation. On Northern blot the transcript is detected at about 5KD. Expression of SEQ ID NO:1 is found in prostate but is absent or at very low levels, in brain, heart, kidney, spleen, liver, colon, lung, small intestine, muscle, stomach, testis, placenta, salivary gland, thyroid, adrenal gland, pancreas, ovary, uterus, skin, peripheral blood leucocytes, bone marrow, fetal brain and fetal liver. The polynucleotide is present in prostate cancer but in variable amounts (para bridging pages 3-4).

One cannot extrapolate the teaching of the specification to the enablement of the claims because it cannot be determined from the information in the specification, for the reasons set forth above, whether SEQ ID NO:1 is differentially expressed in primary tumor cells as compared to normal primary control cells, or whether the noncoded mRNA has any functions associated with the cited mRNAs or whether the Alu-like sequences are sufficiently homologous to Alu sequences to function as suggested. Thus, it is unknown and cannot be predicted, without undue

experimentation, whether or not SEQ ID NO:1 is in any way associated with prostate cancer or could be used in any of the suggested diagnostic, therapeutic methods or assay methods. Further, even if the "variability" of expression disclosed were to be found to be different that the expression of SEQ ID NO:1 in normal primary control prostate cells as compared to primary prostate cancer cells, there is no teaching in the specification as to what is meant by differential expression, for the reasons set forth above. The only thing that is clear from the specification is that SEQ ID NO:1 is expressed in both prostate and prostate cancer cells. What those cells are or where they come from is not disclosed. The specification provides no information on the source of SEQ ID NO:1 or the source of the tumor cells which were assayed to determine the "variable" expression of SEQ ID NO:1. In particular, if SEQ ID NO:1 were isolated from, for example, a cultured cell line and then assayed in cultured prostate tumor cell lines, the artifactural nature of cell lines is well known in the art and it could not be determined whether the "variability" of SEQ ID NO:1, if indeed its expression is different from SEQ ID NO:1 in primary prostate tumor cells as compared with normal controls, is in any way related to the *in vivo* cells from which the cell line was derived in view of the art recognized problems with artifacts associated with cell culture. Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary-type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to

one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Thus, if the claimed invention is based on the cell culture data, it could not be predicted that, in the *in vivo* environment, expression of SEQ ID NO:1 would in any way be correlated with prostate cancer. Further, Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded. This is exemplified by the teachings of Zellner et al (Clin. Can. Res., 1998, 4:1797-1782) who specifically teach that products are over expressed in glioblastoma (GBM)-derived cell lines which are not over expressed *in vivo*. Drexler et al further teach that only a few cell lines containing cells that resemble the *in-vivo* cancer cells have been established and even for the bona fide cancer cell lines it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Further, Embleton et al (Immunol Ser, 1984, 23:181-207) specifically teaches that in procedures for the diagnosis of osteogenic sarcoma, caution must be used when interpreting results obtained with monoclonal antibodies that had been raised to cultured cell lines and specifically teach that cultured tumor cells may not be antigenically typical of the tumor cell population from which they were derived and it is well established that new

artifactual antigens can occur as a result of culture (see attached abstract). Hsu (in Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures *in vitro* frequently change their chromosomal constitutions (see abstract). It is clear that the unpredictability of using cancer cell lines is well known in the art since Slamon et al, (Cancer Cells, 1989, 7:371-384) specifically teach that for their studies they use clones from actual human tumor tissue because DNA in cell lines can acquire genetic changes *in vitro* that may not be representative of the gene *in vivo*, p. 373, col 1). Thus, if based on cell culture data, in the absence of objective data provided from primary tumor cells and normal controls, no one of skill in the art would believe it more likely than not that the claimed invention would have any correlation with any aspect of prostate cancer.

In addition as drawn to the non-coding regions, there is no teaching in the specification as to which functions these regions could be used for. In the absence of further guidance, one would not know how to use these regions. Further, as drawn to the Alu-type sequences in anti-sense orientation, there is no teaching of how the sequence could be used to "modulate" or even whether or not they are sufficiently homologous to ALU sequences so that they could be used as probes to detect and quantitate Alu sequences or even "modulate" those sequences.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict how to use the "novel" polynucleotide, SEQ ID NO:1 with a reasonable

expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

9. If Applicant were able to overcome the rejections under 35 USC 101 and 35 USC 112, first paragraph above, Claims 1 and 18 would still be rejected under 35 USC 112, first paragraph because the specification while enabling for SEQ ID NO:1, does not reasonably provide enablement for complements of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to complements of a polynucleotide that is selectively expressed in prostate. The specification teaches as set forth above.

One cannot extrapolate the teaching of the specification to the scope of the claims because it is conventional and well known in the art, as taught by US Patent No. 5,912,143 that the term complementary refers to the natural binding of polynucleotides under permissive salt and temperature conditions and specifically teaches that complementarity between two single-stranded molecules may be "partial" or it may be "complete" (col 5, lines 19-32). When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a substantial number of the complementary polynucleotides encompassed by the claims **would not** share either structural or functional properties with SEQ ID NO:1 or encode proteins that share either structural or functional properties with the protein encoded by SEQ ID NO:1. The specification fails to

provide an enabling disclosure for how one would use such polynucleotides. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art on how to use the broadly claimed species. For the above reasons, undue experimentation would be required to practice the claimed invention.

10. Claims 1, 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1 and therefore the written description is not commensurate in scope with the claims drawn to complements of SEQ ID NO:1 and fragments of SEQ ID NO:1 which comprise the nucleotide sequence of PR33a from nucleotide positions 1763-5198.

The claims are drawn to complements of SEQ ID NO:1 which is selectively expressed in prostate and complements of fragments of SEQ ID NO:1 which comprise the nucleotide sequence of PR33a from nucleotide positions 1763-5198.

The specification discloses an isolated cDNA sequence, SEQ ID NO: 1. The claims, as written, however, encompass polynucleotides which vary substantially in length and also in nucleotide composition. Because the claims do not recite hybridization conditions, the broadly claimed genus of complements additionally, encompasses genes, as well as genes incorporating only portions of the disclosed sequence.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses genes. The art

indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (see Harris et al, J. Am. Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising the claimed broadly complements.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a specific nucleotide sequence, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

11. Claims 1, 2, 3 and 18 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitations of "comprises the nucleotide sequence of PR33a from nucleotide positions 1-5198" and "comprises the nucleotide sequence of PR33a from nucleotide positions 1763-5198" have no clear support in the specification and the claims as originally filed. A review of the specification did not reveal any mention of the claimed ranges of nucleic acid residues. The subject matter claimed in claims 1, 2, 3 and 18 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13 Claims 1 and 18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Boehringer Mannheim Biochemicals, 1994 Catalog, p. 93).

The claims are drawn to a complements of SEQ ID NO:1 residues 1763-5198 wherein said SEQ ID NO:1 is selectively expressed in prostate. The claims are also drawn to complements of probes wherein the probes are selected from SEQ ID NO:1, positions 1763-5198, wherein said probes are at least 8 contiguous residues.

Boehringer Mannheim teaches random primers that encompass all possible 6-nucleotide sequences (see page 93, Catalog No. 1034 731/1006 924), and therefore a subset of the random primers would include complements of SEQ ID NO:1 residues 1763-5198 which is selectively expressed in prostate and complements of probes that are at least 8 nucleotides in length selected from residues 1763-5198 of SEQ ID NO:1. All of the limitations of the claims are met.

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
September 29, 2003